Figure 1

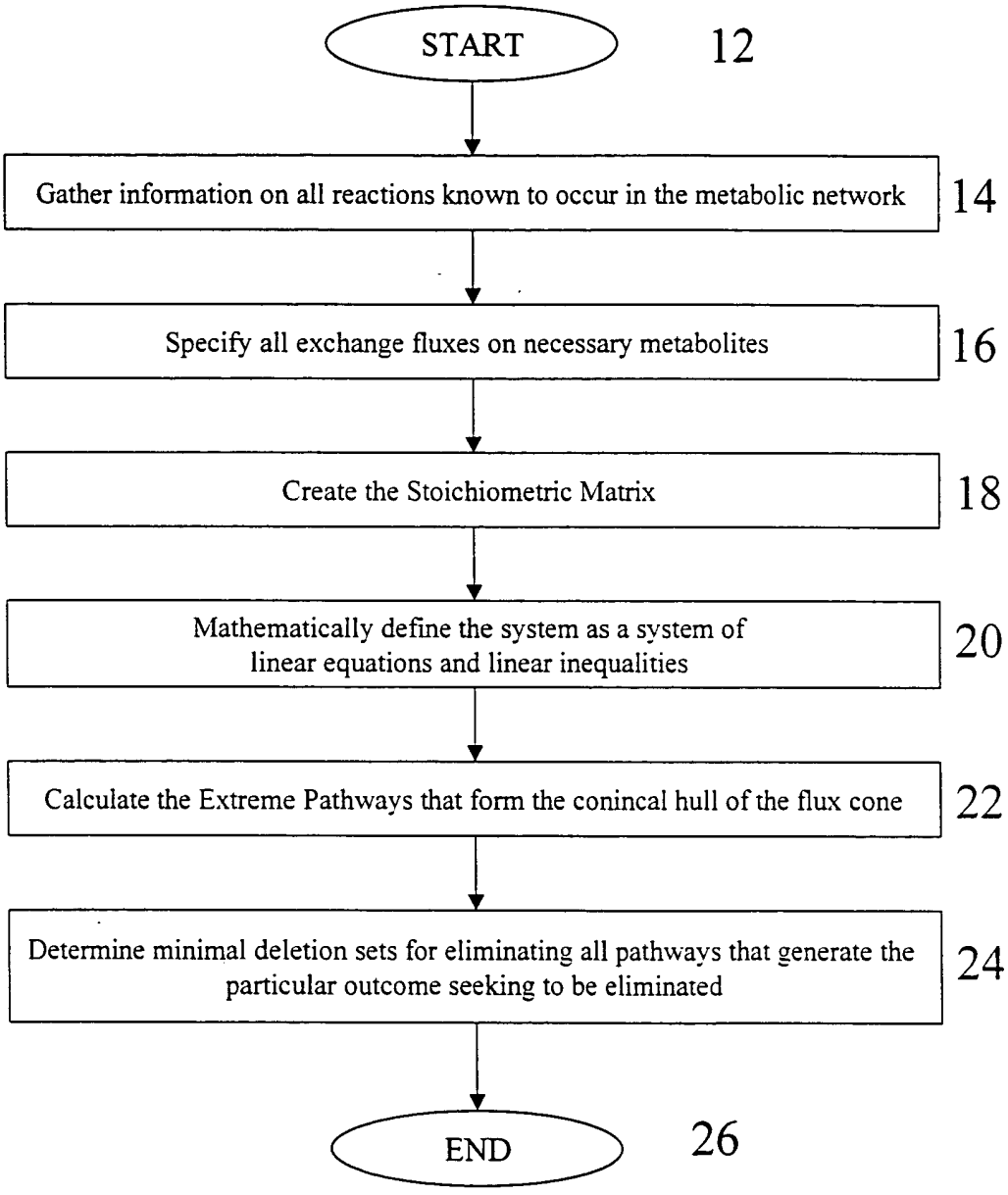

START
12
Gather information on all reactions known to occur in the metabolic network
14
Specify all exchange fluxes on necessary metabolites
16
Create the Stoichiometric Matrix
18
Mathematically define the system as a system of linear equations and linear inequalities
20
Calculate the Extreme Pathways that form the conincal hull of the flux cone
22
Determine minimal deletion sets for eliminating all pathways that generate the particular outcome seeking to be eliminated
24
END
26

Figure 2

Convex Analysis		Cellular Biology
Convex Hull		Capabilities of a Metabolic Genotype
Unique Generating Vectors		Systemically Independent Extreme Pathways
Particular Solution		Metabolic Phenotype
Flux Vector		Combination of Active Extreme Pathways

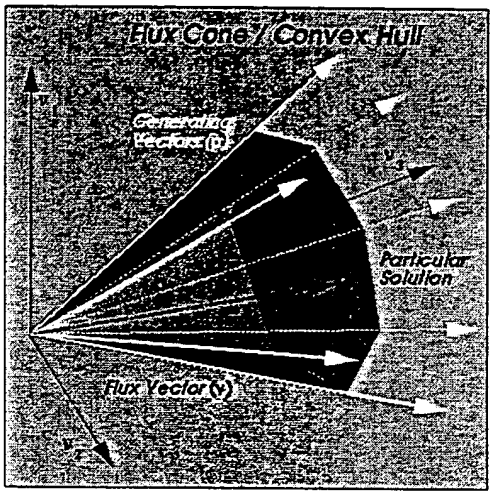
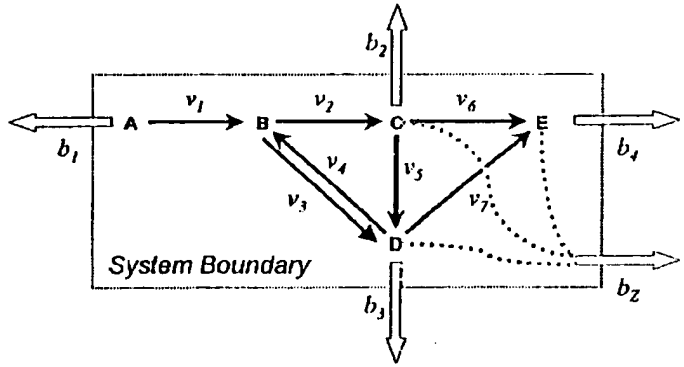


Figure 3

(A) Example Metabolic Reaction Scheme *(Linked Outputs)*



Internal Fluxes

v_1: A → B
v_2: B → C
v_3: B → D
v_4: D → B
v_5: C → D
v_6: C → E
v_7: 2D → E

Exchange Fluxes

b_1: A →
b_2: C →
b_3: D →
b_4: E →
b_Z: C + D + 2E →

(B) Mathematical Representation

Steady State Mass Balances

A: $-v_1 - b_1 = 0$
B: $v_1 + v_4 - v_2 - v_3 = 0$
C: $v_2 - v_5 - v_6 - b_2 - b_Z = 0$
D: $v_3 + v_5 - v_4 - 2v_7 - b_3 - b_Z = 0$
E: $v_6 + v_7 - b_4 - 2b_Z = 0$

Flux Constraints

$0 \le v_1, \ldots, v_7 \le +\infty$
$-\infty \le b_1 \le 0$
$-\infty \le b_2 \le 0$
$0 \le b_3 \le 0$
$0 \le b_4 \le 0$
$0 \le b_Z \le +\infty$

(C) Extreme Pathways

Pathway	*Internal Fluxes*							*Exchange Fluxes*				
Number	v_1	v_2	v_3	v_4	v_5	v_6	v_7	b_1	b_2	b_3	b_4	b_z
p'_1	5	0	5	0	0	0	2	-5	-1	0	0	1
p'_2	1	0	1	0	0	2	0	-1	-3	0	0	1
p'_3	0	0	0	0	5	0	2	0	-6	0	0	1
p'_4	0	0	0	0	1	2	0	0	-4	0	0	1
p'_5	6	1	5	0	0	0	2	-6	0	0	0	1
p'_6	4	3	1	0	0	2	0	-4	0	0	0	1
p'_7	6	6	0	0	5	0	2	-6	0	0	0	1
p'_8	4	4	0	0	1	2	0	-4	0	0	0	1
p'_9	0	0	1	1	0	0	0	0	0	0	0	0
p'_{10}	0	1	0	1	1	0	0	0	0	0	0	0

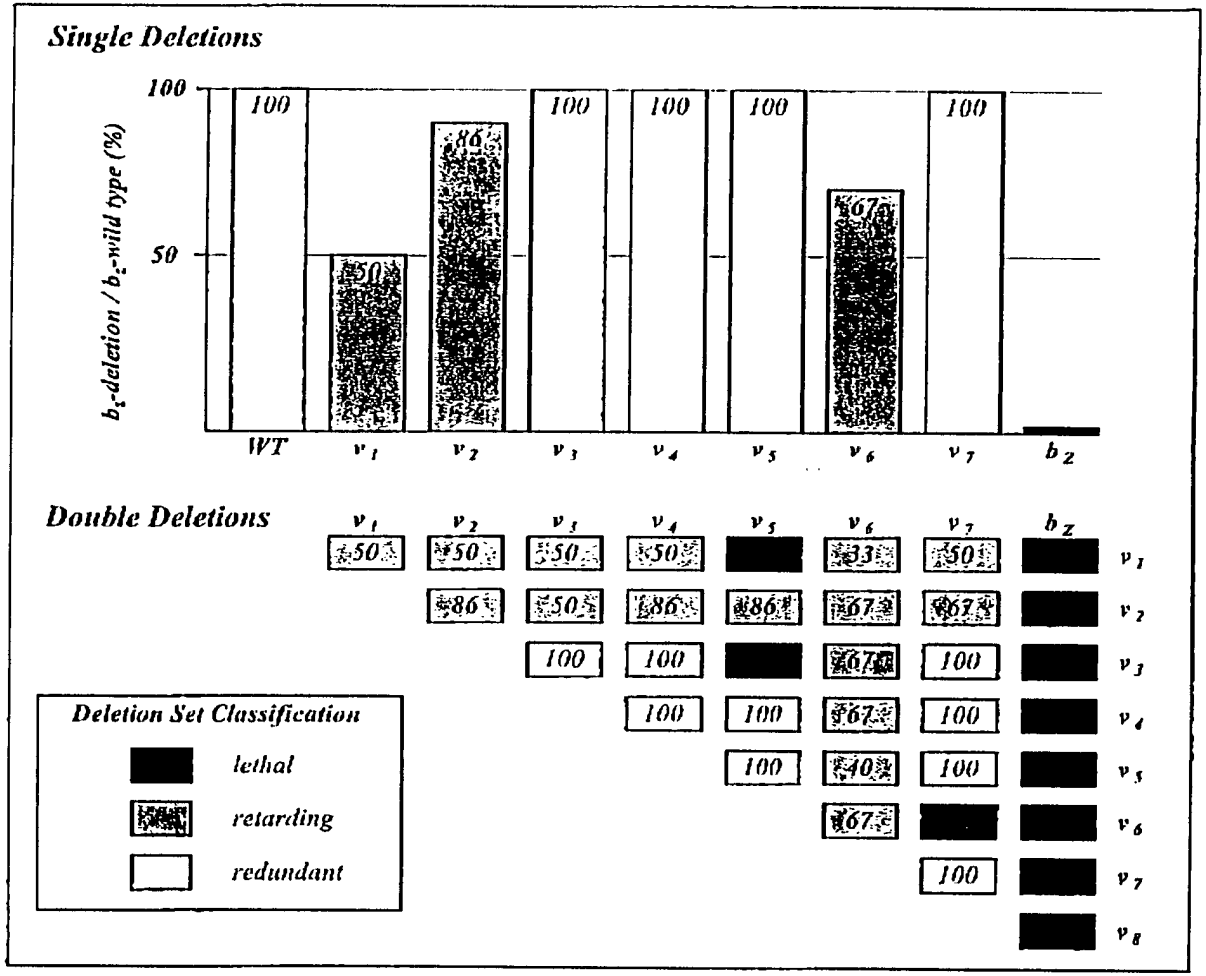
Figure 4

Table 1

Pathway Number	Internal Fluxes								Exchange Fluxes		
	v_1	v_2	v_3	v_4	v_5	v_6	v_-	v_8	b_1	b_2	b_3
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	0	0	0	0	3	0	2	1	0	-4	1
4	0	0	0	0	1	2	0	1	0	-4	1
5	4	1	3	0	0	0	2	1	-4	0	1
6	4	3	1	0	0	2	0	1	-4	0	1
7	4	4	0	0	3	0	2	1	-4	0	1
8	4	4	0	0	1	2	0	1	-4	0	1
9	0	0	1	1	0	0	0	0	0	0	0
10	0	1	0	1	1	0	0	0	0	0	0

Table 1: The set of extreme pathways (p1,...,p10) for the reaction scheme depicted in Figure 2. Pathway 1 and 2 correspond to pathways utilizing both metabolite A and C as substrates, while pathway 3 and 4 utilize only metabolite C. Pathway 5, 6, 7, and 8 utilize metabolite A as the sole substrate. Pathway 9 and 10 show no activity in the exchange fluxes and correspond to internal cycles.

Figure 5


Single Deletions
100
50
b_z-deletion / b_z-wild type (%)
100
50
86
100
100
100
67
100
WT
v_1
v_2
v_3
v_4
v_5
v_6
v_7
b_2
Double Deletions
v_1 v_2 v_3 v_4 v_5 v_6 v_7 b_2
50 50 50 50 33 50 v_1
86 50 86 86 67 67 v_2
100 100 67 100 v_3
100 100 67 100 v_4
100 40 100 v_5
67 v_6
100 v_7
v_8
Deletion Set Classification
lethal
retarding
redundant